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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/930,283	08/16/2001	Usha Kasid	P 0280652 KAUS430501	9971
23460	7590	02/25/2004	EXAMINER	
LEYDIG VOIT & MAYER, LTD TWO PRUDENTIAL PLAZA, SUITE 4900 180 NORTH STETSON AVENUE CHICAGO, IL 60601-6780			GIBBS, TERRA C	
			ART UNIT	PAPER NUMBER
			1635	18

DATE MAILED: 02/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/930,283	Applicant(s) KASID ET AL.	
	Examiner Terra C. Gibbs	Art Unit 1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on 24 November 2003.

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) 1-10 and 12-27 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) 1-10 and 12-27 is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) ☐ All b) ☐ Some * c) ☐ None of:
 1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date <u>17</u> .	4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. _____. 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) 6) <input type="checkbox"/> Other: _____.
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DETAILED ACTION

This Office Action is a response to Applicants Amendment, filed February 24, 2003, Applicants Response, filed June 6, 2003 and Applicants Amendment, filed November 24, 2003.

Claim 11 has been canceled. Claims 4, 9, 15, 16, 26, and 27 have been amended. New claims 26 and 27 are acknowledged.

Claims 1-10 and 12-27 are pending in the instant application.

Claims 1-10 and 12-27 have been examined on the merits.

Information Disclosure Statement

The Information Disclosure Statement, filed November 24, 2003 is acknowledged. The information referred to therein has been considered on the merits.

Specification

Applicants Amendment to the Abstract to comply with the Sequence Rules, filed November 24, 2003 is acknowledged.

Oath/Declaration

The new Oath, to correct for deficiencies, filed June 11, 2003 is acknowledged.

Nucleotide and/or Amino Acid Sequence Disclosure

Amendments to the claims to identify sequences throughout the disclosure with appropriate SEQ ID NO. is acknowledged.

Claim Objections

The amendment to claim 4 is remove an extra "C" in the nucleotide sequence to properly characterize it as SEQ ID NO:1 is acknowledged.

Double Patenting

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1-8 and 17 were rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 2, 5, 6, 8 and 13 of U.S. Patent No. 6,126,965 ('965 patent). **This rejection is maintained** for the reasons of record set forth in the previous Office Action, filed October 23, 2003.

In response to this rejection, Applicants argue that the double patenting rejection of these claims is improper. Applicants rely on M.P.E.P at §804, Subsection II. Applicants contend the since the pending application is a continuation of an abandoned divisional application of the '965 patent, a double patenting rejection is improper. This is not found persuasive because Applicant's reliance on M.P.E.P at §804, Subsection II is not applicable to the nonstatutory double patenting rejection of record against claims 1-8 and 17. The Examiner assumes that Applicants are specifically relying on the fact that a double patenting rejection is not permitted where the claimed subject matter is presented in a divisional application as a result of a restriction requirement made in a parent applicant under 35 U.S.C. 121. When reviewing the parent application, USSN 08/957,327, now '965 patent, a restriction requirement was indeed made. However, the restriction requirement was made between the liposomal **composition**

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comprising an antisense oligonucleotide and the **method** of radiosensitizing a tumor using an antisense composition. Therefore M.P.E.P at §804, Subsection II, is not relevant to the nonstatutory double patenting rejection of record against claims 1-8 and 17, and is therefore proper.

Claims 9, 10, and 12-15 were rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-6 of U.S. Patent No. 6,333,314 ('314 patent). **This rejection is maintained** for the reasons of record set forth in the previous Office Action, filed October 23, 2003.

In response to this rejection, Applicants argue that claims 9-15 of the instant application are patentably distinct from claims 1-6 of the '314 patent. Applicants argues that claim 1 of the '314 patent incorporates the limitation of a composition of a cationic liposome, phosphatidylcholine, and cholesterol, whereas claims 9, 10, and 12-15 of the instant application do not require such elements to carry out their method use. This is not found persuasive because the *species* of the '314 patent anticipates the *genus* claims 9, 10, and 12-15 of the instant application. See MPEP § 2131.02.

Claim 16 was rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 7 of U.S. Patent No. 6,333,314. **This rejection is maintained** for the reasons of record set forth in the previous Office Action, filed October 23, 2003.

In response to this rejection, Applicants argue that claim 16 of the instant invention recites a pharmaceutically acceptable carrier and a generic composition of liposome. This is not found persuasive because a pharmaceutically acceptable carrier can be simply water and therefore the *species* of the '314 patent anticipates the *genus* claim 16 of the instant application. Applicant is directed to MPEP § 2131.02.

Claims 18-20 were rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. 6,333,314. **This rejection is maintained** for the reasons of record set forth in the previous Office Action, filed October 23, 2003.

In response to this rejection, Applicants argue that claims 18-20 are patentably distinct from claim 1 of the '314 patent. Applicants argue that claim 19 of the instant application recites oncogenes (ras, raf, cot, mos, and myc) which are not recited by the claims of the '314 patent. This is not found persuasive because while claim 1 of the '314 patent does not explicitly recite an oncogene *per se*, the claim recites SEQ ID NO:1, which is an antisense oligonucleotide targeted to the oncogene c-raf. Furthermore, claim 18 is so broad to include "a method of radiosensitizing tumor tissue by administration of a radiosensitizing amount of one antisense oligonucleotide [**containing**] the sequence SEQ ID NO:1". The term "containing is open-language, and therefore the composition of the instant claims is encompassed in the '314 patent. Therefore, the method of radiosensitizing tumor tissue of the instant application overlaps in scope with the method of radiosensitizing tumor tissue of the '314 patent.

Applicant is reminded, a timely filed terminal disclaimer in compliance with 37 CFR 1.321(c), may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Claim Rejections - 35 USC § 112

Claims 18-25 were rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of administering antisense raf of the nucleotide sequence 5'-GTGCTCCATTGATGC-3' intratumorally in immunocompromised mice, does not reasonably provide enablement for the radiosensitization of any tumor in an organisms wherein an oligonucleotide is administered *in vivo*. **This rejection is withdrawn** in view of the new 35 U.S.C. 112, first paragraph enablement rejection presented below.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 18-27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an improved method of treating a patient having cancerous tumor tissue, comprising the administration of therapeutic radiation, wherein the improvement comprises sensitizing said cancerous tumor tissue by administration of a composition comprising a cationic liposome, phosphatidylcholine, and cholesterol, and further comprises an encapsulated antisense oligonucleotide of no more than 40 bases containing SEQ ID NO:1, does not

reasonably provide enablement for an improved method of treating a patient having cancerous tumor tissue comprising the administration of therapeutic radiation wherein the improvement comprises sensitizing said cancerous tumor tissue by the administration of a radiosensitizing composition comprising a cationic liposome, phosphatidylcholine, and cholesterol, and further comprises *any* encapsulated oncogene antisense oligonucleotide of no more than 40 bases. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or the invention commensurate in scope with these claims.

This is a new rejection.

The claimed invention is drawn to an (improved) method of treating cancer comprising the administration of therapeutic radiation and further comprising the administration of a radiosensitizing composition comprising a cationic liposome, phosphatidylcholine, cholesterol, and an antisense oligonucleotide of no more than 40 bases, specific to an oncogene, to a whole organism *in vivo*.

The specification teaches the inhibition of raf expression target cells *in vitro* upon the administration of raf antisense, as well as cell survival studies *in vitro* following cellular irradiation and antisense administration. The specification additionally teaches the resulting distribution profiles of raf antisense following its intravenous administration into Balb/c mice, whereby antisense degradation is minimized upon liposome encapsulation and raf expression is decreased in target cells.

At the time the instant invention was made, the therapeutic use of antisense oligonucleotides was a highly unpredictable art due to obstacles that continue to hinder the therapeutic application of antisense *in vivo* (whole organism). For example, Branch (TIBS,

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February 1998 Vol. 23, pages 45-50) teaches that "because it is very difficult to predict what portions of an RNA molecule will be accessible *in vivo*, effective antisense molecules must be determined empirically by screening large number of candidates for their ability to act inside cells."; "Binding is the rare exception rather than the rule, and antisense molecules are excluded from most complementary sites. Since accessibility cannot be predicted, rational design of antisense molecules is not possible."; and, "The relationship between accessibility to oligonucleotide (ODN) binding and vulnerability to ODN-mediated antisense inhibition *in vivo* is beginning to be explored...It is not yet clear whether *in vitro* screening techniques...will identify ODN's that are effective *in vivo*."

The specification does not teach a method of treating a patient having cancerous tumor tissue, improved or otherwise, using a radiosensitizing composition comprising a cationic liposome, phosphatidylcholine, cholesterol, and *any* oncogenic antisense oligonucleotide, other than the antisense oligonucleotide of SEQ ID NO:1. One skilled in the art would not accept on its face the examples given in the specification of the distribution profiles of raf antisense following its intravenous administration into Balb/c mice, whereby antisense degradation is minimized upon liposome encapsulation and raf expression is decreased in target cells, as being correlative or representative of a method of treating a patient having cancerous tumor tissue, improved or otherwise, using a radiosensitizing composition comprising a cationic liposome, phosphatidylcholine, cholesterol, and *any* oncogenic antisense oligonucleotide, particularly in view of the lack of guidance in the specification and known unpredictability associated with the delivery of antisense nucleic acids *in vivo*, as cited in the references of Branch as discussed above. The specification as filed fails to provide any particular guidance which resolves the

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known unpredictability associated with the rational design of antisense molecules and treatment effects provided by antisense administered in a whole organism.

The claims are so broad to include an (improved) method of treating any cancer tissue comprising the administration of *any* oncogenic antisense oligonucleotide, where the specification has only taught SEQ ID NO:1. Given the art-recognized unpredictability of the therapeutic application of antisense *in vivo*, the determination of such factors as differences in target site accessibility, dosage, route of administration, disposition of the antisense molecule in tissues, and the half life and stability of the antisense molecule *in vivo*, would not be routine and would require undue trial and error experimentation.

Due to the lack of specific guidance in the specification as filed and the unpredictability of using antisense oligonucleotides *in vivo* and the unpredictability associated with the rational design of antisense molecules, one of skill in the art would require specific guidance to practice the current invention. The current specification does not provide such guidance to an (improved) method of treating a patient having cancerous tumor tissue comprising the administration of therapeutic radiation wherein the improvement comprises sensitizing said cancerous tumor tissue by the administration of any radiosensitizing composition comprising a cationic liposome, phosphatidylcholine, cholesterol, and an oncogenic antisense oligonucleotide, and one of skill in the art would be required to perform trial and error or undue experimentation.

Therefore, based on the breadth of the claims, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, the amount of direction or guidance presented, the presence or absence of working examples of the invention, and the quantity of experimentation that would be required, it would require undue

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experimentation, beyond what is taught in the specification, to practice the methods over the full scope claimed without undue trial and error experimentation.

It is noted that in response to the 35 U.S.C. 112, first paragraph rejection against claims 18-25 for scope enablement in the previous Office Action, Applicants argued that the instant specification disclosed ubiquitous localization and sustainability of liposome oligonucleotides sufficiently enable those skilled in the art to radiosensitive radio resistant tumors in accord with the method of claims 18-25. Applicants point the Examiner to the instant specification at page 18, lines 18-17, where liposome encapsulated oligodeoxyribonucleotides were detected up to 48 hours post administration, and were detected in all organs. This is not found persuasive because Applicants provide data for a liposome encapsulated raf-1 oligodeoxyribonucleotide (SEQ ID NO:1), however, no evidence has been provided in the instant specification, for the successful treatment, improved or otherwise, using any other oligodeoxyribonucleotides. The claims are so broad to include any oncogenic antisense oligonucleotide, where only raf-1 (SEQ ID NO:1) is taught. Applicants have provided no *in vivo* evidence that an improved cancer treatment has been provided comprising the administration of therapeutic radiation and further comprising the administration any antisense oligonucleotide, other than SEQ ID NO:1. Therefore, the teachings of the specification are not commensurate in scope with the claimed invention comprising an improved treatment for any and/or all types of cancers using any oncogenic antisense oligonucleotide.

Claims 9-15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of radiosensitizing tumor tissue by administration of a

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composition comprising a cationic liposome, phosphatidylcholine and cholesterol, and further comprising an encapsulated antisense oligonucleotide of no more than 40 bases containing SEQ ID NO:1, does not reasonably provide enablement for a method of radiosensitizing tumor tissue by administration of radiosensitizing effective amount of at least one antisense oligonucleotide of no more than 40 bases containing SEQ ID NO:1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or the invention commensurate in scope with these claims. **This is a new rejection.**

Claims 9-15 are drawn to a method of radiosensitizing tumor tissue by administration of radiosensitizing effective amount of at least one antisense oligonucleotide of no more than 40 bases containing SEQ ID NO:1.

The specification teaches the inhibition of raf expression target cells *in vitro* upon the administration of raf antisense, as well as cell survival studies *in vitro* following cellular irradiation and antisense administration. The specification additionally teaches the resulting distribution profiles of raf antisense following its intravenous administration into Balb/c mice, whereby antisense degradation is minimized upon liposome encapsulation and raf expression is decreased in target cells.

The instant specification, at page 18, lines 12-17 teach findings that suggest the oligonucleotides with only the end bases phosphorothioated are rapidly degraded *in vivo* and that liposome encapsulation using the liposomes of the invention protect the oligonucleotide from degradation for at least 48 hours. Additionally, the instant specification, at page 26, lines 1-3, discloses, "the liposomes of the invention provide significant protection of antisense oligonucleotides against degradation in blood and normal tissue".

Gokhale et al. (Gene Therapy, 1997 Vol. 4:1289-1299) (Applicants reference AG) teach, "By simultaneously measuring plasma and tissue levels, we also demonstrate that liposomal encapsulation of oligos protects these relatively small pieces of DNA from degradation in plasma and facilitates their tissue accumulation. "Circulating antisense raf oligos carried *in vivo* by liposomes were intact for at least 24h, while free oligos were undetectable after 5 minutes" (see page 1295, second column).

Given the disclosures of the instant invention of the teachings of Gokhale et al. one of skill in the art would conclude that *intact* SEQ ID NO:1 would be rapidly degraded by nucleases and would not accumulate to any tumor tissue to radiosensitive said tumor tissue as contemplated in the instant specification. Therefore, in view of applicant's admissions, in addition to teachings in the prior art, it is apparent that *liposome encapsulation* of SEQ ID NO:1 is necessary to practice the methods over the full scope claimed without undue trial and error experimentation.

Claim Rejections - 35 USC § 102

Claim 1 was rejected under 35 U.S.C. 102(b) as being anticipated by Epand et al. [U.S. Patent No. 5,283,185]. **This rejection is maintained** for the reasons of record set forth in the previous Office Action, filed October 23, 2003.

In response to this rejection, Applicants argue that Epand et al. notes that the cationic lipid used in the method disclosed therein "has a structure which includes lipophilic groups derived from cholesterol" (column 3, lines 12-13). Applicants argue that Epand et al. do not disclose a liposome containing cholesterol and, therefore, does not anticipate claim 1. This is not

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found persuasive because while Epand et al. disclose that cationic lipid has a structure which includes a lipophilic groups derived from cholesterol, Epand et al. further disclose that the cationic lipid is, for example, 3 β -[N-(polyethyleneimine)-carbamoyl] cholesterol (see column 3, line 35).

Therefore, Epand et al. anticipate claim 1.

Claim Rejections - 35 USC § 103

Claims 18-25 were rejected under 35 U.S.C. 103(a) as being unpatentable over Patel et al. (Molecular Carcinogenesis, 1993 Vol. 8:7-12), Kasid et al. (Science, 1989 Vol. 243:1354-1356), Monia et al. [U.S. Patent No. 5,952,229] in further view of Epand et al. [U.S. Patent No. 5,283,185] and Seung et al. (Cancer Research, 1995 Vol. 55:5561-5565). **This rejection is withdrawn** in view of the Applicants arguments that Seung et al. teaches away from the present invention.

Conclusions

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Terra C. Gibbs whose telephone number is (571) 272-0758. The examiner can normally be reached on M-F 9:00-5:00.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on (571) 272-0760. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

tcg
February 19, 2004


KAREN A. LACOURCIERE, PH.D
PRIMARY EXAMINER

Notice of References Cited	Application/Control No. 09/930,283	Applicant(s)/Patent Under Reexamination KASID ET AL.	
	Examiner Terra C. Gibbs	Art Unit 1635	Page 1 of 1

U.S. PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	Classification
	A	US-			
	B	US-			
	C	US-			
	D	US-			
	E	US-			
	F	US-			
	G	US-			
	H	US-			
	I	US-			
	J	US-			
	K	US-			
	L	US-			
	M	US-			

FOREIGN PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Country	Name	Classification
	N					
	O					
	P					
	Q					
	R					
	S					
	T					

NON-PATENT DOCUMENTS

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
	U	Branch, A. A Good Antisense is Hard to Find. TIBS, February 1998 Vol. 23, pages 45-50.
	V	
	W	
	X	

*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)
Dates in MM-YYYY format are publication dates. Classifications may be US or foreign.

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Substitute for form 1449A/B/PTO		Complete if Known	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use as many sheets as necessary)		Application Number	09/930,283
		Filing Date	August 16, 2001
		First Named Inventor	Kasid et al.
		Group Art Unit	1635
		Examiner Name	Terrea C. Gibbs
Sheet 1 of 1	Attorney Docket Number	219603	

U.S. PATENT DOCUMENTS						
Examiner Initials	Doc. No.	U.S. Patent Document		Name of Patentee or Applicant	Date of Publication	Filing Date if Appropriate
		Application or Patent Number	Kind Code			
JP	AA	5,641,662		Debs et al.	June 24, 1997	
	AB	5,696,277		Hosteller et al.	Dec. 9, 1997	
	AC	5,827,703		Debs et al.	Oct. 27, 1998	
	AD	6,120,798		Allen et al.	Sep. 19, 2000	
JP	AE	6,248,351	B1	Xing et al.	June 19, 2001	

FOREIGN PATENT DOCUMENTS								
Examiner Initials	Doc. No.	Foreign Patent Document			Name of Patentee or Applicant	Date of Publication	Translation	
		Office	Application or Patent Number	Kind Code			Yes	No**

OTHER - NON PATENT LITERATURE DOCUMENTS						
Examiner Initials	Doc. No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number (s), publisher, city and/or country where published.				Translation
						Yes No**
LP	AF	GOKHALE et al., "Enhanced inhibition of Raf-1 kinase by liposomal antisense raf oligodeoxyribonucleotide in human squamous carcinoma cells," <i>American Asso. Cancer Research</i> , 37, Poster Section 6 #2807 (1996)				
	AG	GOKHALE et al., "Antisense raf oligodeoxyribonucleotide is protected by liposomal encapsulation and inhibits Raf-1 protein expression in vitro and in vivo: implication for gene therapy of radioresistant cancer," <i>Gene Therapy</i> , 4, 1289-1299 (1997)				
	AH	GOKHALE et al., "Antisense raf Oligodeoxyribonucleotide Is a Radiosensitizer <i>In Vivo</i> ," <i>Antisense & Nucleic Acid Drug Development</i> , 9, 191-201 (1999)				
	AI	LITZINGER et al., "Fate of cationic liposomes and their complex with oligonucleotide in vivo," <i>Biochimica et Biophysica Acta</i> , 1281, 139-149 (1996)				
	AJ	MAHER et al., "Specific Hybridization Arrest of Dihydrofolate Reductase mRNA in Vitro Using Anti-sense RNA or Anti-sense Oligonucleotides," <i>Archives of Biochemistry and Biophysics</i> , 253, 214-220 (1987)				
LP	AK	SOLDAATENKOV et al., "Inhibition of Raf-1 Protein Kinase by Antisense Phosphorothioate Oligodeoxyribonucleotide Is Associated with Sensitization of Human Laryngeal Squamous Carcinoma Cells to Gamma Radiation," <i>Cancer J. Sci. Am.</i> , 3, 13-20 (1997)				

Examiner Signature	<i>Terrea C. Gibbs</i>	Date Considered	2/16/04
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- * A concise statement of relevance is being submitted in lieu of a translation. 37 CFR 1.98(a)(3).
- + An English-language equivalent/patent, or an English-language abstract, or an English-language version of the search report or action by a foreign patent office in a counterpart foreign application indicating the degree of relevance found by the foreign office is being submitted in lieu of a concise explanation of relevance under 37 CFR 1.98(a)(3).